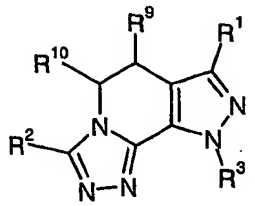
Claims

1. An inhaled combination of (a) a selectiv PDE4 inhibitor of the formula (I)

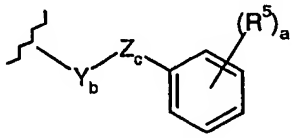


(I)

or a pharmaceutically acceptable salt or solvate thereof, wherein:

R^1 is H, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_2-C_4) alkenyl, phenyl, -$N(CH_3)_2$, (C_3-C_6) cycloalkyl, (C_3-C_6) cycloalkyl(C_1-C_3) alkyl or (C_1-C_6) acyl, wherein the alkyl, phenyl or alkenyl groups may be substituted with up to two -OH, (C_1-C_3) alkyl, or -CF_3 groups or up to three halogens;

R^2 and R^3 are each independently selected from the group consisting of H, (C_1-C_{14}) alkyl, (C_1-C_7) alkoxy(C_1-C_7) alkyl, (C_2-C_{14}) alkenyl, (C_3-C_7) cycloalkyl, (C_3-C_7) cycloalkyl(C_1-C_2) alkyl, a saturated or unsaturated (C_4-C_7) heterocyclic$(CH_2)_n$ group wherein n is 0, 1 or 2, containing as the heteroatom one or two of the group consisting of oxygen, sulfur, sulfonyl, nitrogen and NR^4 where R^4 is H or (C_1-C_4) alkyl; or a group of the Formula (II):



(II)

wherein a is an integer from 1 to 5; b and c are 0 or 1; R^5 is H, -OH, (C_1-C_5) alkyl, (C_2-C_5) alkenyl, (C_1-C_5) alkoxy, (C_3-C_6) cycloalkoxy, halogen, -CF_3, -CO_2R^6, -$CONR^6R^7$, -NR^6R^7, -NO_2, or -$SO_2NR^6R^7$ wherein R^6 and R^7 are each independently H, or (C_1-C_4) alkyl; Z is -O-, -S-, -SO_2-, -CO- or -$N(R^8)$- wherein R^8 is H or (C_1-C_4) alkyl; and Y is (C_1-C_5) alkylene or (C_2-C_6) alkenylene optionally substituted with up to two (C_1-C_7) alkyl or (C_3-C_7) cycloalkyl groups; wherein each

of the alkyl, alkenyl, cycloalkyl, alkoxyalkyl or heterocyclic groups may be substituted with 1 to 14, preferably 1 to 5, (C_1-C_2) alkyl, CF_3, or halo groups; and

R^9 and R^{10} are each independently selected from the group consisting of H, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_6-C_{10}) aryl and (C_6-C_{10}) aryloxy;

and (b) an adrenergic β2 receptor agonist.

2. A combination as claimed in claim 1 wherein R^1 is methyl, ethyl or isopropyl.

3. A combination as claimed in claim 1 or claim 2 wherein R^3 is (C_1-C_6) alkyl, (C_2-C_6) alkenyl, (C_3-C_7) cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_6)alkyl or phenyl optionally susbtituted with 1 or 2 of the group consisting of H, -OH, (C_1-C_5) alkyl, (C_2-C_5) alkenyl, (C_1-C_5) alkoxy, halogen, trifluoromethyl, $-CO_2R^6$, $-CONR^6R^7$, $-NR^6R^7$, $-NO_2$ or $-SO_2NR^6R^7$ wherein R^6 and R^7 are each independently H or (C_1-C_4) alkyl.

4. A combination as claimed in any one of the preceding claims wherein the selective PDE4 inhibitor of the formula (I) is selected from:

9-cyclopentyl-5,6-dihydro-7-ethyl-3-phenyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopenyl-5,6-dihydro-7-ethyl-3-(furan-2-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-pyridyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(4-pyridyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(3-thienyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

3-benzyl-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-propyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

3,9-dicyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(1-methylcyclohex-1-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

3-(*tert*-butyl)-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-methylphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-methoxyphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(thien-2-yl)-9*H*-pyrazolo[3,4-*c*]1,2,4-triazolo[4,3-α]pyridine;

3-(2-chlorophenyl)-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-iodophenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-trifluoromethylphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine; and

5,6-dihydro-7-ethyl-9-(4-fluorophenyl)-3-(1-methylcyclohex-1-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3-α]pyridine;

and the pharmaceutically acceptable salts and solvates thereof.

5. A combination as claimed in claim 4 wherein the selective PDE4 inhibitor of the formula (I) is selected from 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-thienyl)-9*H*-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-α]pyridine and 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(*tert*-butyl)-9*H*-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-α]pyridine and the pharmaceutically acceptable salts and solvates thereof.

6. A combination as claimed in any one of the preceding claims wherein the adrenergic β2 receptor agonist is selected from salmeterol, formoterol and the pharmaceutically acceptable salts and solvates thereof.

7. A combination as claimed in claim 1 wherein:

the selective PDE4 inhibitor of the formula (I) is 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-thienyl)-9*H*-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-α]pyridine, or a pharmaceutically acceptable salt or solvate thereof, and the adrenergic β2 receptor agonist is salmeterol, or a pharmaceutically acceptable salt or solvate thereof;

the selective PDE4 inhibitor of the formula (I) is 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-thienyl)-9*H*-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-α]pyridine, or a pharmaceutically acceptable salt or solvate thereof, and the adrenergic β2 receptor agonist is formoterol, or a pharmaceutically acceptable salt or solvate thereof;

the selective PDE4 inhibitor of the formula (I) is 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(*tert*-butyl)-9*H*-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-α]pyridine, or a pharmaceutically acceptable salt or solvate thereof, and the adrenergic β2 receptor agonist is salmeterol, or a pharmaceutically acceptable salt or solvate thereof; or

the selective PDE4 inhibitor of the formula (I) is 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(*tert*-butyl)-9*H*-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-α]pyridine, or a pharmaceutically acceptable salt or solvate thereof, and the adrenergic β2 receptor agonist is formoterol, or a pharmaceutically acceptable salt or solvate thereof.

8. A combination as claimed in any preceding claim for use as a medicament.

9. A combination as claimed in any one of claims 1 to 7 for simultaneous, sequential or separate administration in the treatment of an obstructive airways or other inflammatory disease.

10. A pharmaceutical composition comprising a selective PDE4 inhibitor of the formula (I), as defined in claim 1, an adrenergic β2 receptor agonist and a pharmaceutically acceptable excipient, diluent or carrier, for administration by the inhaled route in the treatment of an obstructive airways or other inflammatory disease.

11. A pharmaceutical composition as defined in claim 10 wherein the selective PDE4 inhibitor of the formula (I) and the adrenergic β2 receptor agonist are as defined in any one of claims 2 to 7.

12. The use of a selective PDE4 inhibitor of the formula (I), as defined in claim 1, or an adrenergic β2 receptor agonist in the manufacture of a medicament for simultaneous, sequential or separate administration of both agents by the inhaled route in the treatment of an obstructive airways or other inflammatory disease.

13. The use of claim 12 wherein the selective PDE4 inhibitor of the formula (I) and the adrenergic β2 receptor agonist are as defined in any one of claims 2 to 7.

14. A method of treating of an obstructive airways or other inflammatory disease comprising administering simultaneously, sequentially or separately, by the inhaled route, to a mammal in need of such treatment, an effective amount of a selective PDE4 inhibitor of the formula (I), as defined in claim 1, and an adrenergic β2 receptor agonist.

15. A method as claimed in claim 14 wherein the selective PDE4 inhibitor of the formula (I) and the adrenergic β2 receptor agonist are as defined in any one of claims 2 to 7.

16. An inhalation device for simultaneous, sequential or separate administration of a selective PDE4 inhibitor of the formula (I), as defined in claim 1, and an adrenergic β2 receptor agonist in the treatment of an obstructive airways or other inflammatory disease.

17. An inhalation device as claimed in claim 16 wherein the selective PDE4 inhibitor of the formula (I) and the adrenergic β2 receptor agonist are as defined in any one of claims 2 to 7.